MAIL STOP APPEAL BRIEF
PATENT
2503-1215

IN THE U.S. PATENT AND TRADEMARK OFFICE

In re application of	Appeal No.
Ezio BOMBARDELLI	Conf. 1808
Application No. 10/580,190	Group 1655
Filed May 23, 2006	Examiner Qiuwen Mi

COMPOSITIONS FOR THE TREATMENT OF AFFECTIONS OF THE ORAL CAVITY AND UPPER RESPIRATORY TRACT

APPEAL BRIEF

MAY IT PLEASE YOUR HONORS:

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1. Real Party in Interest

THE REAL PARTY IN INTEREST IN THIS APPEAL IS:

INDENA S.P.A., VIALE ORTLES 12, I-20139 MILANO, ITALY.

2. Related Appeals and Interferences

NONE.

3. Status of Claims

Claims 2-5 and 16 have been canceled. Claims 1, 6-15 and 17-25 are pending in the application and stand rejected, from which this appeal is taken.

4. Status of Amendments

No amendments have been filed subsequent to the final rejection mailed May 13, 2010. The claims at issue are thus those set forth in the Amendment filed May 4, 2009.

5. Summary of Claimed Subject Matter

Independent claim 1: As is set forth in independent claim 1, the present invention pertains to compositions that include:

a) anthocyanosides, procyanidins and phloroglucinols;

b) anthocyanosides and phloroglucinols; and

c) procyanidins and phloroglucinols (Page 1, lines 14-17), for the treatment of the affections of the oral cavity and upper respiratory tract (Page 1, lines 18-19), wherein

the anthocyanosides are derived from *Vaccinium myrtillus* extract (Page 1, lines 24-25),

the procyanidins are derived from a *Vitis vinifera* extract, a *Camellia sinensis* extract or from other edible plants containing the procyanidins (page 2, lines 8-11), and

the phloroglucinols are derived from *Hypericum spp.*, *Myrtus spp.* or *Humulus lupulus* extracts (page 2, lines 16-19) , and wherein the compositions contain at least one of:

100 mg of the anthocyanosides,

100 mg of the procyanidins, or

100 mg of the phloroglucinols (Page 1, lines 20-22).

Independent claim 15: As is set forth in independent claim 15, the present invention pertains to a method for the preparation of a medicament for treatment of affections of the

oral cavity and upper respiratory tract (Page 4, lines 4-8), which includes:

administering to a patient in need thereof an effective amount of a medicament containing (Page 1, lines 5-12):

a) anthocyanosides, procyanidins, and phloroglucinols;

b) anthocyanosides, and phloroglucinols; and

c) procyanidins and phloroglucinols (Page 1, lines 14-17), wherein

the anthocyanosides are derived from *Vaccinium myrtillus* extract (Page 1, lines 24-25),

the procyanidins are derived from a *Vitis vinifera* extract, a *Camellia sinensis* extract or from other edible plants containing the procyanidins (page 2, lines 8-11), and

the phloroglucinols are derived from *Hypericum spp.*, *Myrtus spp.* or *Humulus lupulus* extracts (page 2, lines 16-18),

and wherein the medicament contains at least one of:

100 mg of the anthocyanosides,

100 mg of the procyanidins, or

100 mg of the phloroglucinols (Page 1, lines 20-22).

Independent claim 24: As is set forth in the independent claim 24, the present invention pertains to compositions which include:

b) anthocyanosides and phloroglucinols; and

c) procyanidins and phloroglucinols (Page 1, lines 16-17), for the treatment of the affections of the oral cavity and upper respiratory tract(Page 1, lines 18-19) , wherein

the anthocyanosides are derived from *Vaccinium myrtillus* extract(Page 1, lines 24-25),

the procyanidins are derived from a *Vitis vinifera* extract, a *Camellia sinensis* extract or from other edible plants containing the procyanidins (page 2, lines 8-11), and

the phloroglucinols are derived from *Hypericum spp.*, *Myrtus spp.* or *Humulus lupulus* extracts (page 2, lines 16-18),

and wherein the compositions contain at least one of:

100 mg of the anthocyanosides,

100 mg of the procyanidins, or

100 mg of the phloroglucinols (Page 1, lines 20-22).

Independent claim 25: as is set forth in independent claim 25, the present invention pertains to a method for the preparation of a medicament for treatment of affections of the oral cavity and upper respiratory tract (page 4, lines 4-8), which includes:

administering to a patient in need thereof an effective amount of a medicament containing as active principle (page 1, lines 5-12):

a) anthocyanosides, procyanidins, and phloroglucinols;

b) anthocyanosides, and phloroglucinols; and

c) procyanidins and phloroglucinols (Page 1, lines 15-17), wherein

the anthocyanosides are derived from *Vaccinium myrtillus* extract (Page 1, lines 24-25),

the procyanidins are derived from a *Vitis vinifera* extract, a *Camellia sinensis* extract or from other edible plants containing the procyanidins (page 2, lines 8-11), and

the phloroglucinols are derived from *Hypericum spp.*, *Myrtus spp.* or *Humulus lupulus* extracts (page 2, lines 16-18),

and wherein the medicament contains at least one of:

the anthocyanosides, the procyanidins or the phloroglucinols in an amount effective to induce synergy (Page 3, lines 7-9).

6. Grounds of Rejection to be Reviewed on Appeal

The **first** ground for review on appeal is whether claims 1, 6-15 and 17-25 are unpatentable under 35 U.S.C. §112, first paragraph, as being failing to comply with the written description requirement.

The **second** ground for review on appeal is whether claims 1, 6-15, and 17-25 are sufficiently unpatentable under 35 U.S.C. §112, second paragraph, as being indefinite.

The **third** ground for review on appeal is whether claims 1, 6-8, 15, 17-19, 24 and 25 are sufficiently unpatentable over GIAMPAPA (U.S. 5,895,652), in view of TAGASHIRA et al. (Tagashira et al., Antioxidative activity of hop bitter acids and their analogues, *Bioscience, biotechnology, and biochemistry*, (1995 Apr) Vol. 59, No.4, pp. 740-2), in order to support an allegation of unpatentability under 35 U.S.C. §103.

The **fourth** ground for review on appeal is whether claims 1, 6-8, 13-15, 17-19, 24, and 25 are sufficiently unpatentable over GIAMPAPA and TAGASHIRA et al. and further in view of MIMICA-DUKIC et al. (Mimica-Dukic et al., Antimicrobial and antioxidant activities of three Mentha species essential oils, *Planta medica*, (2003 May) Vol. 69, No.5, pp. 413-9), in order to support an allegation of unpatentability under 35 U.S.C. §103.

The **fifth** ground for review on appeal is whether claims 1, 11, 12, 15, 17, and 22-25 are sufficiently unpatentable over GIAMPAPA, in view of ROSA et al. (Rosa et al., Antioxidant activity of oligomeric acylphloroglucinols from Myrtus communis L., *Free radical research*, (2003 Sep) Vol. 37, No.9, pp. 1013-9), in order to support an allegation of unpatentability under 35 U.S.C. §103.

The **sixth** ground for review on appeal is whether claims 1, 9, 10, 15, 17, 20, 21, 24, and 25 are sufficiently unpatentable over GIAMPAPA, in view of TRIPATHI et al. (Tripathi et al., Antioxidant property of Hypericum perforatum (L.) of Indian origin and its comparison with established Medhya rasayanas [Bacopa monnieri and Nardostachys jatamansi] of Ayurvedic medicine, *Current Science*, (1999) Vol. 76, No.1, pp. 27-29), in order to support an allegation of unpatentability under 35 U.S.C. §103.

7. Argument

7.0 Summary of Argument

The claimed compositions for treating oral affections of the oral cavity and upper respiratory tract are supported and patentable over the applied art. The unexpected results are commensurate in scope with the claims and therefore dissipate any unpatentability that could be alleged.

7.1 First Ground - Written Description

Claims 1, 15 and 24 recite "100 mg of the anthocyanosides, 100 mg of the procyanidins, or 100 mg of the phloroglucinols." The Office asserts that there is no support for the "100 mg" limitations.

However, page 1, lines 20-22 of the specification teaches 1 to 200 mg of the anthocyanosides, 1 to 200 mg of the procyanidins, and 1 to 200 of the phloroglucinols. The 100 mg limitation (although not explicitly stated) is clearly within the 1 to 200 mg range.

The propriety of the "100 mg" limitations is clearly supported by case law.

For example, in *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976), the ranges described in the original specification included a range of "25% - 60%" and specific examples of "36%" and "50%." A corresponding new claim limitation to "at least 35%" did not meet the description requirement because the phrase "at least" had no upper limit

and caused the claim to read literally on embodiments outside the "25% to 60%" range, however a limitation to "between 35% and 60%" did meet the description requirement.

Therefore, a value within a range is proper even if it is not explicitly set forth in the specification.

Withdrawal of this rejection is accordingly indicated.

7.2 Second Ground - Rejection Under 35 U.S.C. §112, Second Paragraph

Claim 1 of the present invention typically recites compositions comprising:

"a) anthocyanosides, procyanidins and phloroglucinols;

b) anthocyanosides and phloroglucinols; ***and***

c) procyanidins and phloroglucinols, for the treatment of the affections of the oral cavity and upper respiratory tract . . ."

Independent claims 15, 24 and 25 set forth similar "and" linking of recitations.

The Office asserts that the Appellant is only entitled to claim one invention in a claim, not three different ones as a combined group of compositions that is not in an alternative form, and Applicant does not have the support to have a kit comprising three compositions.

However, the Amendment of May 4, 2009 changed the alternative "or" to the cumulative "and" term in order to

better reflect the unexpected results set forth in the Declaration, including combinations of A+B+C and B+C such as is set forth in Tables 1 and 2.

Therefore, whether if "or" as originally presented or "and" as amended is used to set forth the present invention, the claims are clear, definite and have full antecedent basis.

However, the "or" limitation can be restored upon indication of allowable subject matter.

Withdrawal of this rejection is accordingly indicated

7.3 Third Ground - Rejection Over GIAMPAPA and TAGASHIRA et al.

The present invention pertains to compositions for treatment of affections of the oral cavity and upper respiratory tract, containing:

a) anthocyanosides, procyanidins, and phloroglucinols;

b) anthocyanosides, and phloroglucinols; and

c) procyanidins and phloroglucinols.

As is set forth in independent claims 1 and 15 of the present invention: "the anthocyanosides are derived from *Vaccinium myrtillus* extract, the procyanidins are derived from a *Vitis vinifera* extract, a *Camellia sinensis* extract or from other edible plants containing them, and the phloroglucinols are derived from *Hypericum spp.*, *Myrtus spp.* or *Humulus*

lupulus extracts." Independent claims 1 and 15 also set forth that the compositions contain at least one of: 100 mg of the anthocyanosides, 100 mg of the procyanidins, or 100 mg of the phloroglucinols.

GIAMPAPA pertains to providing nutritional supplements. GIAMPAPA does not pertain to treating affectations of the oral cavity and is thus non-analogous art. The Office refers to claim 1 of GIAMPAPA, which starts at column 10, line 33 and extends to column 15. The Office more specifically points to subparagraph (c) of claim 1, which recites:

> **(c) a herbal anti-oxidant complex, including: grape seed extract, 95% proanthcyanidin, 20 mg., bilberry extract, 25% anthocyanin, 10 mg., and milk thistle extract, 20 mg.;**

The Office (at page 7 of the Office Action of May 13, 2010) admits that GIAMPAPA does not teach the incorporation of phloroglucinols derived from *Hypericum spp.*, *Myrtus spp.* or *Humulus lupulus* extracts; neither does Giampapa teach the composition contain at least one of 100 mg anthocyanosides, 100 mg of the procyanidins, or 100 mg of the phloroglucinols; or the claimed amount of humulones and lupulones in alpha acid or beta-acids.

The Office turns to TAGASHIRA et al. to address these deficiencies of GIAMPAPA.

TAGASHIRA et al. pertain to hop bitter acids. These can include humulones (1) and lupulones (2) (which is analogized to phloroglucinol). These were shown to have DPPH

radical scavenging activity (RSA) and lipid peroxidation inhibitory activity (LIA) (see Abstract). TAGASHIRA et al. also teach the radical scavenging activity of humulone and lupulone are nearly equivalent to those of two natural antioxidant, alpha-tocopherol and ascorbic acid. As for lipid peroxidation, humulone and lupulone are superior to natural antioxidants by about 10-100 times (page 740, 2nd paragraph, 3rd paragraph).

However, neither GIAMPAPA nor TAGASHIRA et al. disclose or infer compositions for treatment of affections of the oral cavity and upper respiratory tract, such as are set forth in independent claims 1, 15, 24 and 25 of the present invention. These references particularly do not disclose or infer the "100 mg" limitation of the independent claims.

One of ordinary skill would accordingly fail to produce independent claims 1, 15, 24 or 25 of the present invention from a knowledge of GIAMPAPA nor TAGASHIRA et al., and a *prima facie* case of unpatentability has thus not been made. Claims depending upon claims 1, 15, 24 or 25 are patentable for at least the above reasons.

Moreover, a Declaration demonstrating unexpected results has been made of record in the application (see attachment).

The Declaration set forth experimental results that were found to be convincing in the written opinion issued by

the EPO. The Declaration set forth the experimentation reproduced below.

Six groups of 20 patients of both sexes suffering from acute bacterial pharyngitis and throat pain were enrolled.

The patients were treated with ***100 mg*** of the single active principle (either anthocyanosides, procyanidins or phloroglucinol) three times a day for 3 days.

Before and at 60 min after the last treatment the patients were asked to assess pain intensity (P.I) according to the following 6-point (0-5) scale:

0 = no pain,

1= hardly any pain,

2 = moderate pain,

3 = moderately severe pain,

4 = severe pain,

5 = very severe pain.

Moreover, hyperaemia of pharynx and tonsils was also evaluated according to a 4-point scale (absent = 0, slight = 1, moderate = 2, severe 3). The results are reported in Table 1.

TABLE 1

	P.I.		Inflammation of pharynx and tonsils	
	Basal Value	**After treatment**	**Basal Value**	**After treatment**
Vaccinium myrtillus extract (A)	4.7	4.0	2.8	1.9
Vitus vinefera extract (B)	4.5	4.1	2.8	2.0
Mirtus Communis extract (C)	4.6	4.2	2.9	2.2
Composition containing B+C	4.6	2.5	2.8	0.7
Composition containing A+B+C	4.7	1.7	2.9	0.1
Placebo	4.6	4.4	2.9	2.8

At the same time, the patients proceeded with a 20s gargling with 10 ml sterile distilled water followed by the collection of samples.

The samples were adequately diluted with Ringer's solution containing O.2% dithiothreitol, and 0.5 ml of each dilution were spread on 4 agar plates (Columbia) supplemented with 5% sheep blood. The plates were incubated in a CO_2 atmosphere for 72 h for anaerobic culture. After incubation the number of colonies was counted. The results are reported in Table 2.

TABLE 2

	Bacterial count ($x10^5$) in gargling samples	
	Basal Value	**After treatment**
Vaccinium myrtillus extract (A)	20.2	15.2
Vitus vinefera extract (B)	21.4	16.9
Mirtus Communis extract (C)	21.0	17.2
Composition containing B+C	23.2	4.9
Composition containing A+B+C	22.9	2.6
Placebo	23.6	22.4

It should be noted that the experiments reported in the Declaration were carried out using dosages of ***100 mg*** each. The Declaration provides convincing evidence that the three compounds in a 1:1:1 ratio by weight have synergistic effects. It is logical that only the weight ratio is critical for synergy whereas the actually selected dosage may depend upon the patient's weight and sex as well as on other factors. It does not accordingly seem logical to exclude from the claims dosages ranging in the same order of magnitude, such as 110, 150, 180 mg etc.

The results set forth in the Declaration are accordingly commensurate in scope with the claims. Moreover, these unexpected results should be considered in light of the

"and" language or reciting the components set forth in the claims.

Any unpatentability that may be alleged over the applied art is thus dissipated by the unexpected results.

Moreover, the results in the Declaration should not be considered as mere rebuttal evidence but also in light of the failure of the applied art to specifically point to treatment of affectations of the oral cavity.

That is, both the inability to establish *prima facie* obviousness and the unexpected results should be viewed synergistically as establishing patentability of the claimed invention. "The determination of obviousness, *vel non*, requires that all the evidence be considered together . . . if rebuttal evidence of adequate weight is produced, a holding of *prima facie* obviousness, being but a legal inference from previously uncontradicted evidence, is dissipated. The objective evidence of unobviousness is not evaluated for its 'separate knockdown ability' against the 'stonewall' of the *prima facie* case . . . but is considered together with all other evidence, in determining whether the invention is as a whole would have been obvious to a person of ordinary skill in the field of the invention." (citations omitted). *Applied Materials Inc. v. Advanced Semiconductor Materials*, 98 F.3d 1563, 1574, 40 USPQ2d 1481, 1486 (Fed. Cir. 1996).

Withdrawal of this rejection is accordingly indicated.

7.4 – Fourth Ground – GIAMPAPA, TAGASHIRA et al. and MIMICA-DUKIC et al.

MIMICA-DUKIC et al. pertain to antimicrobial and antioxidant activities of three Mentha species essential oils. The oils were tested to evaluate their free radical scavenging ability.

The Office asserts that one of skill in the art to incorporate the oils of MIMICA-DUKIC et al. to enhance the antioxidant activity of GIAMPAPA.

However, there is still not teaching or inference of treating affectations of the oral cavity.

Therefore, even if the teachings of MIMICA-DUKIC et al. were added, there is not teaching or inference of treating affectations of the oral cavity.

Even if for the sake of argument these references could be combined to produce a *prima facie* case of unpatentability, this unpatentability would be dissipated by the unexpected results, especially in regards to the "100 mg" recitations.

This rejection should accordingly be withdrawn.

7.5 Fifth Ground – GIAMPAPA and ROSA et al.

GIAMPAPA has been discussed above.

At page 11 the Office Action of May 11, 2010 acknowledges that GIAMPAPA does not teach the incorporation of phloroglucinols derived from *Hypericum spp.*, *Myrtus spp.* or *Humulus lupulus* extracts; and neither does GIAMPAPA teach the

composition contain at least one of 100 mg anthocyanosides, 100 mg of the procyanidins, or 100 mg of the phloroglucinols; incorporation of phloroglucinols from *Myrtus communis*, or the claimed amount of *Myrtus communis* or the extraction condition of *Myrtus communis* in claims 11 and 22.

The Office turns to ROSA et al.

Rosa et al teach the use of myrtle (*Myrtus communis L.*) as a culinary spice and as a flavoring agent for alcoholic beverages is widespread in the Mediterranean area, and especially in Sardinia. ROSA et al. does not pertain to the treatment of affectations of the oral cavity. Instead, ROSA et al. gave results of studies that established semimyrtucommulone as a dietary antioxidant (see Abstract).

Therefore, even if the teachings of ROSA et al. were added to GIAMPAPA, there is not teaching or inference of treating affectations of the oral cavity.

Even if for the sake of argument these references could be combined to produce a *prima facie* case of unpatentability, this unpatentability would be dissipated by the unexpected results, especially in regards to the "100 mg" recitations.

This rejection should accordingly be withdrawn.

7.6 Sixth Ground GIAMPAPA and TRIPATHI et al.

GIAMPAPA has been discussed above.

At page 14 the Office Action of May 11, 2010 acknowledges that GIAMPAPA does not teach the incorporation of

phloroglucinols derived from *Hypericum spp.*, *Myrtus spp.* or *Humulus lupulus* extracts; and neither does GIAMPAPA teach the composition contain at least one of 100 mg anthocyanosides, 100 mg of the procyanidins, or 100 mg of the phloroglucinols; or the claimed amount of phloroglucinols in *Hypericum perforatum* extract.

TRIPATHI et al. is turned to address these deficiencies.

TRIPATHI et al. pertains to the antioxidant property of *Hypericum perforatum* extract. TRIPATHI et al. concludes that this plant could be used as an antioxidant in medicine (page 27, 2nd column, 2nd paragraph).

There is no teaching or inference in GIAMPAPA and TRIPATHI et al. of treating affectations of the oral cavity.

Therefore, even if the teachings of TRIPATHI et al. were added to GIAMPAPA, there is not teaching or inference of treating affectations of the oral cavity.

Even if for the sake of argument these references could be combined to produce a *prima facie* case of unpatentability, this unpatentability would be dissipated by the unexpected results, especially in regards to the "100 mg" recitations.

This rejection should accordingly be withdrawn.

8. Conclusion

The Appellant has demonstrated that the Examiner has failed to successfully allege that the rejected claims are new matter, indefinite or *prima facie* unpatentable. It is clear that the inventive compositions for treatment of affections of the oral cavity and upper respiratory tract represent a truly inventive technology, as is evidenced by the unexpected results. For the reasons advanced above, it is respectfully submitted that all the rejected claims in this application are allowable. Thus, favorable reconsideration and reversal of the rejections of the under 35 USC §§112/103, by the Honorable Board of Patent Appeals and Interferences, are respectfully solicited.

As an Appeal Brief has been previously filed on March 24, 2010, no fee is due for the instant Appeal Brief. See MPEP 1207.04.

Respectfully submitted,

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October 21, 2010
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Enclosures: Claims Appendix
Evidence Appendix

9. Claims Appendix

1. Compositions comprising:

a) anthocyanosides, procyanidins and phloroglucinols;

b) anthocyanosides and phloroglucinols; and

c) procyanidins and phloroglucinols, for the treatment of the affections of the oral cavity and upper respiratory tract, wherein

the anthocyanosides are derived from *Vaccinium myrtillus* extract,

the procyanidins are derived from a *Vitis vinifera* extract, a *Camellia sinensis* extract or from other edible plants containing the procyanidins, and

the phloroglucinols are derived from *Hypericum spp.*, *Myrtus spp.* or *Humulus lupulus* extracts,

and wherein the compositions contain at least one of:

100 mg of the anthocyanosides,

100 mg of the procyanidins, or

100 mg of the phloroglucinols.

6. The compositions as claimed in claim 1, wherein the phloroglucinols are derived from *Hypericum perforatum* or *Myrtus communis* extracts, or from *Humulus lupulus* fractions enriched in α and β acids.

7. The compositions as claimed in claim 6, wherein the β acids fraction from *Humulus lupulus* contains 20 to 80% of phloroglucinols expressed as colupulone, and the α acids contains 20 to 80% of humulone.

8. The compositions as claimed in claim 7, wherein the β acids fraction prepared from *Humulus lupulus* contains 60% of phloroglucinols expressed as colupulone, and the α acids contains 60% of humulone.

9. The compositions as claimed in claim 1, wherein the *Hypericum sp.* extracts include a *Hypericum perforatum* extract with a phloroglucinols content ranging from 20 to 80%.

10. The compositions as claimed in claim 9, wherein the phloroglucinols content of the *Hypericum perforatum* extract is 60%.

11. The compositions as claimed in claim 6, wherein the *Myrtus communis* extract is prepared from leaves of *Myrtus communis* by extraction with carbon dioxide under conditions of pressure ranging from 235 to 260 bars and temperatures ranging from 40 to 60°C.

12. The compositions as claimed in claim 11, wherein the *Myrtus communis* extract has a content in myrtucommulone of 35%.

13. The compositions as claimed in claim 1, further containing at least one essential oil.

14. The compositions as claimed in claim 13, wherein the essential oil is mint oil.

15. A method for the preparation of a medicament for treatment of affections of the oral cavity and upper respiratory tract, which comprises:

administering to a patient in need thereof an effective amount of a medicament containing:

a) anthocyanosides, procyanidins, and phloroglucinols;

b) anthocyanosides, and phloroglucinols; and

c) procyanidins and phloroglucinols, wherein

the anthocyanosides are derived from *Vaccinium myrtillus* extract,

the procyanidins are derived from a *Vitis vinifera* extract, a *Camellia sinensis* extract or from other edible plants containing the procyanidins, and

the phloroglucinols are derived from *Hypericum spp.*, *Myrtus spp.* or *Humulus lupulus* extracts,

and wherein the medicament contains at least one of:

100 mg of the anthocyanosides,

100 mg of the procyanidins, or

100 mg of the phloroglucinols.

17. The method as claimed in claim 15, wherein the phloroglucinols are derived from *Hypericum perforatum* or *Myrtus communis* extracts, or from *Humulus lupulus* fractions enriched in α and β acids.

18. The method as claimed in claim 17, wherein the β acids fraction from *Humulus lupulus* contains 20 to 80% of phloroglucinols expressed as colupulone, and the α acids contains 20 to 80% of humulone.

19. The method as claimed in claim 18, wherein the β acids prepared from *Humulus lupulus* contains 60% of phloroglucinols expressed as colupulone, and the α acids fraction contains 60% of humulone.

20. The method as claimed in claim 1, wherein the *Hypericum sp.* extract is a *Hypericum perforatum* extract with phloroglucinols content ranging from 20 to 80%.

21. The method as claimed in claim 20, wherein the phloroglucinols content of the *Hypericum perforatum* extract is 60%.

22. The method as claimed in claim 17, wherein the *Myrtus communis* extract is prepared from leaves of *Myrtus communis* by extraction with carbon dioxide under conditions of pressure ranging from 235 to 260 bars and temperatures ranging from 40 to 60°C.

23. The method as claimed in claim 17, wherein the *Myrtus communis* extract has a content in myrtucommulone of 35%.

24. Compositions comprising:

b) anthocyanosides and phloroglucinols; and

c) procyanidins and phloroglucinols, for the treatment of the affections of the oral cavity and upper respiratory tract, wherein

the anthocyanosides are derived from *Vaccinium myrtillus* extract,

the procyanidins are derived from a *Vitis vinifera* extract, a *Camellia sinensis* extract or from other edible plants containing the procyanidins, and

the phloroglucinols are derived from *Hypericum spp.*, *Myrtus spp.* or *Humulus lupulus* extracts,

and wherein the compositions contain at least one of:

100 mg of the anthocyanosides,

100 mg of the procyanidins, or

100 mg of the phloroglucinols.

25. A method for the preparation of a medicament for treatment of affections of the oral cavity and upper respiratory tract, which comprises:

administering to a patient in need thereof an effective amount of a medicament containing as active principle:

a) anthocyanosides, procyanidins, and phloroglucinols;

b) anthocyanosides, and phloroglucinols; and

c) procyanidins and phloroglucinols, wherein

the anthocyanosides are derived from *Vaccinium myrtillus* extract,

the procyanidins are derived from a *Vitis vinifera* extract, a *Camellia sinensis* extract or from other edible plants containing the procyanidins, and

the phloroglucinols are derived from *Hypericum spp.*, *Myrtus spp.* or *Humulus lupulus* extracts,

and wherein the medicament contains at least one of:

the anthocyanosides, the procyanidins or the phloroglucinols in an amount effective to induce synergy.

10. Evidence Appendix

An executed Declaration under 37 C.F.R. § 1.132, filed on May 7, 2008 and made of record in the Final Office Action of May 30, 2008.

13818 V
(15-2003)

PATENT
2503-1215

IN THE U. S. PATENT AND TRADEMARK OFFICE

In re application of

Ezio BOMBARDELLI Conf. 1808

Application No. 10/580,190 Group 1655

Filed: May 23, 2006 Examiner Qiuwen Mi

Title: COMPOSITIONS FOR THE TREATMENT OF AFECTIONS OF THE ORAL CAVITY AND UPPER RESPIRATORY TRACT

DECLARATION UNDER 37 C.F.R. § 1.132

1. I, Ezio Bombardelli, a named inventor, am a citizen of Italy and reside at Via Gabetta 13, I-27027 GROPELLO CAIROLI, Italy.

2. I am familiar with the above-identified U.S. patent application, its prosecution before the United States Patent and Trademark Office, and the applied art references of KORNEYEV (U.S. Patent 6,576,269), ZULLI et al. (U.S. Publication 2002/0131942), GHOSAL (U.S. Patent 6,224,906), YALOVENY AGRIC IND (SU 1373398A), NIEUWENHUIZEN et al. (U.S. Publication 2003/0064937), COOPER et al. (U.S. Patent 6,379,720), WALKER et al. (U.S. Patent 5,474,774), IMAOKA et al. (JP 406179609), BARNEY et al. (U.S. Patent 5,370,863), Van DEN BERGHE (U.S. Patent 6,284,289), ZOU (CN 1421240), GORENBEIN et

al. (U.S. Patent 5,955,102) and GIOVANNI et al. (Journal of Natural Products, 65(3):334-8, 2002).

3. In order to demonstrate the patentability of the invention, I offer the following data of unexpected results.

Six groups of 20 patients of both sexes suffering from acute bacterial pharyngitis and throat pain were enrolled.

The patients were treated with 100 mg of the single active principle (either anthocyanosides, procyanidins or floroglucinol) three times a day for 3 days.

Before and at 60 min after the last treatment the patients were asked to assess pain intensity (P.I) according to the following 6-point (0-5) scale:

0 = no pain,

1= hardly any pain,

2 = moderate pain,

3 = moderately severe pain,

4 = severe pain,

5 = very severe pain.

Moreover, hyperaemia of pharynx and tonsils was also evaluated according to a 4-point scale (absent = 0,

slight = 1, moderate = 2, severe 3). The results are reported in Table 1.

TABLE 1

	P.I.		Inflammation of pharynx and tonsils	
	Basal Value	**After treatment**	**Basal Value**	**After treatment**
Vaccinium myrtillus extract (A)	4.7	4.0	2.8	1.9
Vitus vinefera extract (B)	4.5	4.1	2.8	2.0
Mirtus Communis extract (C)	4.6	4.2	2.9	2.2
Composition containing B+C	4.6	2.5	2.8	0.7
Composition containing A+B+C	4.7	1.7	2.9	0.1
Placebo	4.6	4.4	2.9	2.8

At the same time, the patients proceeded with a 20s gargling with 10 ml sterile distilled water followed by the collection of samples.

The samples were adequately diluted with Ringer's solution containing 0.2% dithiothreitol, and 0.5 ml of each dilution were spread on 4 agar plates (Columbia) supplemented with 5% sheep blood. The plates were incubated in a CO_2 atmosphere for 72 h for anaerobic

culture. After incubation the number of colonies was counted. The results are reported in Table 2.

TABLE 2

	Bacterial count ($x10^5$) in gargling samples	
	Basal Value	**After treatment**
Vaccinium myrtillus extract (A)	20.2	15.2
Vitus vinefera extract (B)	21.4	16.9
Mirtus Communis extract (C)	21.0	17.2
Composition containing B+C	23.2	4.9
Composition containing A+B+C	22.9	2.6
Placebo	23.6	22.4

The unexpected results of the invention are thus clear, and any alleged unpatentability is fully rebutted.

It is also noted that these experimental results that were found to be convincing in the written opinion issued by the EPO.

4. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both,

under §1001 of Title 18 of the United States code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date April 22, 2008

Ezio Bombardelli

11. Related Proceedings Appendix

NONE.